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09/354,500

07/16/1999

MACK J. SCHERMER

GSIL-0109-PU

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05/04/2005

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EXAMINER

ALLEN, MARIANNE P

ART UNIT

PAPER NUMBER

1631

DATE MAILED: 05/04/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/354,500

Applicant(s)

SCHERMER ET AL.

Examiner

Marianne P. Allen

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 10-20 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 10-20 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. ____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date ____. | 6) <input type="checkbox"/> Other: ____. |

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DETAILED ACTION

In view of the remand mailed 10/29/04, PROSECUTION IS HEREBY REOPENED.

New grounds of rejection are set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:

(1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(2) request reinstatement of the appeal.

If reinstatement of the appeal is requested, such request must be accompanied by a supplemental appeal brief, but no new amendments, affidavits (37 CFR 1.130, 1.131 or 1.132) or other evidence are permitted. See 37 CFR 1.193(b)(2).

Claim Rejections - 35 USC § 112

Claims 10-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for automatically creating crosstalk-corrected data of a microarray using the exemplified matrix algebra, does not reasonably provide enablement for computing a set of correction factors and applying the set of correction factor to quantitation data obtained from the generated microarray images in any other way. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification on page 9 discloses matrix algebra techniques for creating crosstalk-corrected data of a microarray having three or more dye spots. No other methods or algorithms for computing the set of correction factors from the output measurements and for applying the

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set of correction factors to quantitation data obtained from the generated microarray images are disclosed. The record does not reflect that any other techniques would have been known at the time of the invention. The specification does not point to any other methods nor provide guidance for developing any other techniques for computing these factors. As such, breadth of the claims is not enabled.

Claims 10-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 10 recites “means for measuring an output of each of the output channels,” “means for computing a set of correction factors,” and “means for applying the set of correction factors to quantitation data.” These claim limitations do not appear to fall within the scope of 35 U.S.C. 112, sixth paragraph, as the corresponding structures to perform this function do not appear to be disclosed in the specification. As the specification does not appear to provide the corresponding structures of the means-plus-function limitation such that one skilled in the art would know and understand what structure corresponds to these means limitations, these claims are confusing. Applicant is requested to clarify whether they intended to invoke 35 USC 112, sixth paragraph, and if so to point to the equivalents in the specification. Alternatively, applicant is requested to point to the part of the specification that particularly points out the metes and bounds of the recited means-plus-function elements.

Claim Rejections - 35 USC § 103

Claims 1-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Trulson et al. (U.S. Patent No. 5,578,832) or Brown et al. (U.S. Patent No. 5,807,522) in view of Ginestet (U.S. Patent No. 6,225,636).

Trulson et al. discloses a method and system for correcting data with overlapping dye emission spectra in nucleic acid microarray analysis. Glass slides and fluorescent dyes are particularly disclosed. The microarray is scanned for each dye to produce dye images. The images are deconvoluted using ratios of brightness. A four by four emission cross section matrix is produced. The data is normalized. (See abstract; claims; columns 3-5; Figures 13-19; and columns 22-26.) A problem solved by the reference is how to handle the emission spectral overlap (crosstalk) between the labels. (See column 22, lines 49-56.) Trulson et al. discloses using four fluorescent dyes. While the reference does not explicitly refer to calibration dye spots using a single pure dye, it is reasonable to infer that single pure dye spots were used for calibration as such dye spots appear to have been routine in the art at the time of the invention. (See at least Schermer et al., U.S. Patent No. 6,075,613 at column 2, lines 20-50.)

Brown et al. discloses a method and system for scanning nucleic acid microarrays using two-color fluorescent detection and correcting optical crosstalk caused by overlapping dye emission spectra (see columns 16-17). Glass slides are disclosed. (See column 12, lines 3-5.) The array was scanned using a laser fluorescent scanner. The scanned image was gridded and analyzed using image analysis software. Crosstalk between the fluorophores due to their overlapping emission spectra was corrected. (See column 17, lines 2-4.) While the reference does not explicitly refer to calibration dye spots using a single pure dye, it is reasonable to infer

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that single pure dye spots were used for calibration as such dye spots appear to have been routine in the art at the time of the invention. (See at least Schermer et al., U.S. Patent No. 6,075,613 at column 2, lines 20-50.) In addition, Brown et al. does not disclose use of three or more dyes.

Ginestet discloses M-FISH or multi-fluor fluorescence in situ hybridization and cross-talk compensation for three or more fluorescent dyes. The matrix algebra for the correction factors from pure dye spots are disclosed. (See at least abstract; Figure 8; column 2, lines 30-40; column 5, lines 35-50; and columns 9-11.) Ginestet does not explicitly disclose microarrays or chips containing nucleic acids.

If pure dye spots for calibration were not used in the nucleic acid microarray methods of Trulson et al. or Brown et al. (as appears to have been common practice as evidenced by Schermer et al.), then it would have been obvious to do so given the teachings of Ginestet which explicitly disclosing such pure dyes for calibration to correct cross-talk due to overlapping dye emission spectra in nucleic acid hybridization.

In addition, it would have been obvious to one of ordinary skill in the art to apply the cross-talk correction matrix algebra for three or more dyes as taught by Ginestet to the microarray technology and applications as taught by Trulson et al. and Brown et al. Each of the references make clear that use of fluorescent dyes in nucleic acid hybridization applications was common at the time of the invention and that cross-talk due to overlapping emission spectra was a well known problem. Trulson et al. and Ginestet make clear that using three or more fluorescent dyes was routine and desirable in nucleic acid hybridization applications. It would have been obvious to correct or compensate for cross-talk using techniques well known to those of ordinary skill in the art.

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The recitation of “quantitation” data was introduced into claims 1 and 10 in the amendment filed 10/7/02. This response argued that this “quantitation” limitation distinguished over the art applied. Claims must be interpreted as broadly as their terms reasonably allow. The words of the claim must be given their plain meaning unless applicant has provided a clear definition in the specification. In this case, the specification does not provide a definition for “quantitation data.” Basis for this phrase has been pointed to only in the abstract. As such, the phrase must be read as it would be interpreted by those of ordinary skill in the art. In this art, “quantitation” data is considered to mean data that is quantified in any way. Clearly, each of Trulson et al., Brown et al., and Ginestet quantitate the dye fluorescence data and correct for cross-talk due to overlapping emission spectra based on this quantitation data.

Applicant’s response on page 6 of the brief quotes two references by Schena. “Quantitation is usually accomplished by superimposing a grid.” “Typically, a user-defined gridding pattern is overlaid on the image.” Note that the terms “usually” and “typically” indicate that other methods could have been used. Note that the specification does not reference the Schena (April 1999) document such that one of ordinary skill in the art might have been informed that this was a contemplated embodiment. Note that Schena (January 2000) was published after the effective filing date and would not have been available to one of ordinary skill in the art at the time of the invention. To the degree that applicant believes that the phrase “quantitate data” provides a specific claim limitation requiring the method and system to implicitly include a gridding pattern overlaid on an image, this is not agreed with. Finally, it is noted that Brown et al. specifically discloses that the scanned image was gridded and analyzed

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using image analysis software. Even if the claims could be amended to specifically recite such a limitation, the prior art of record suggests this type of analysis.

Applicant's response on page 8 of the brief states, "The Examiner concedes that this feature is neither taught, disclosed or discussed by any of the prior art references of record taken either alone or in combination with one another." This is disagreed with. Such a concession would mean that no art rejection was applicable and in view of the art rejection of record, applicant has made a clearly incorrect statement. The statement in the final Office action dated 12/24/2002 indicates that the examiner understood applicant's argument about what "quantitation data" meant but did not agree.

On page 6 of the brief, applicant references 56 patents that issued prior to the filing date of the instant application that contained the phrase "quantitation data." The examiner was unable to find any list of the particular patents found. In an effort to be responsive to the remand by the BPAI, the examiner has performed a similar search of U.S. patents issued prior to the filing date of the instant application that contain the phrase "quantitation data." The search identified 112 patents. Sixty were issued prior to the filing date of the instant application. (See attached.) None of the patents was directed to correcting cross-talk of microarray dye emission spectra. Each of the patents was quantitating experimental or biological data in a different manner depending on the nature of the invention. This supports the examiner's position that the phrase "quantitating data" has no special meaning in the instant application, particularly in the absence of a specific definition.

With respect to the means plus function limitations set forth in claims 10-20 ("means for measuring an output of each of the output channels," "means for computing a set of correction

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factors,” and “means for applying the set of correction factors to quantitation data”), the specification does not appear to provide the corresponding structures of the means-plus-function limitations such that one skilled in the art would know and understand what structure corresponds to these means limitations. As such, the examiner has interpreted the claim to mean that any system that accomplishes these three activities is embraced by the claims. As set forth above, the prior art suggests such a system.

In view of the above, the claimed method and system are obvious over the prior art.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marianne P. Allen whose telephone number is 571-272-0712. The examiner can normally be reached on Monday-Thursday, 5:30 am - 1:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, Ph.D., can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.



Marianne P. Allen
Primary Examiner

5/2/05

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mpa

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SUPERVISORY PATENT EXAMINER